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14. ABSTRACT **Background**: Casualty care is challenging because caregivers may be inexperienced, or distracted by environmental dangers or multiple casualties. **Objective:** To provide clinical data for development and validation of a system that executes, in real time, automated decision-assist tools that accurately identify key trauma patient conditions and guide relevant life-saving interventions. This system will be comprised of novel "artificial intelligence" algorithms that only rely on data measured by standard patient transport monitors. **Specific Aims:** We will validate a, fully functional prototype of the decision-assist system, which can be provided to an industry partner for full productization. **Study Design**: We will prospectively trial these algorithms by making use of our operational, IRB-approved "plug-and-play" system for clinical field-testing of algorithms, presently in use on board Boston Medflight helicopters and the MGh Emergency Dept. **Relevance:** Because the necessary medical instrumentation, i.e., a standard travel monitor, is so very familiar to caregivers, these decision-assistance capabilities could be broadly deployed with a relative minimum of additional training, hardware acquisition, and up-front buy-in by clinicians.

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INTRODUCTION

Reviewing the entirety of this program puts the proposed efforts into a context. The entirety of the program's project narrative is therefore provided below. However, the research operations that occur at the Massachusetts General Hospital and Boston Medflight air ambulances are focused on data collection and prospective technology assessments.

1.1. State-of-the-art for patients with substantial bleeding

Hemorrhage is recognized as the most important, treatable cause of death after injury [1, 2]. A recent series of reports [3, 4] has shown improved outcomes when trauma centers employ so-called "substantial bleeding protocols" [5].

Underlying these protocols are two basic strategies. First, damage-control resuscitation (DCR) includes aggressive measures to avoid coagulopathy (via permissive hypotension that slows blood loss, adequate restoration of coagulation factors via transfusion, and minimization of hypothermia). This is very important, because trauma-induced coagulopathy affects between 24 and 56% of critically injured patients [6, 7]. Second, DCR is paired with damage-control surgery, an operative strategy prioritizing early surgical control of bleeding, while sparing non-critical surgical repairs that are undertaken only after the patient has sufficiently recovered.

1.2. An unresolved question: when to initiate the "substantial bleeding protocol"

The care protocols for substantially bleeding patients are resource intensive and time sensitive. It is therefore notable that there is no well-established, evidence-based method about when and how to activate the protocols. Consider two recent reports from centers that have demonstrated mortality benefit of these practices, where the protocols are initiated based on subjective assessments:

- Riskin et al. [3] reported that the Stanford Protocol is activated "*at the discretion of the attending physician*."

- Holcomb and Gumbert [5], who have previously shown mortality benefits of these protocols [4], remark that in their experience, activation is subjective: "The process of activating … varies with each institution. *Generally, on arrival to the emergency department, the attending trauma surgeon evaluates the patient's physiology and injury complex … Once a clinical diagnosis of substantial bleeding is made, the attending clinician activates* [the protocol]."

In theory, there are three reasons to seek an improved, objective method for the initiation of substantial bleeding protocols:

- Centers that are pioneering these protocols are staffed by thought-leaders in the trauma-care world, whose ability to make appropriate subjective decisions may be far superior to typical facilities that lack leading experts. Thus, the benefits of these protocols may not be accrued by centers or facilities that lack caregivers with the expertise necessary to apply them appropriately.

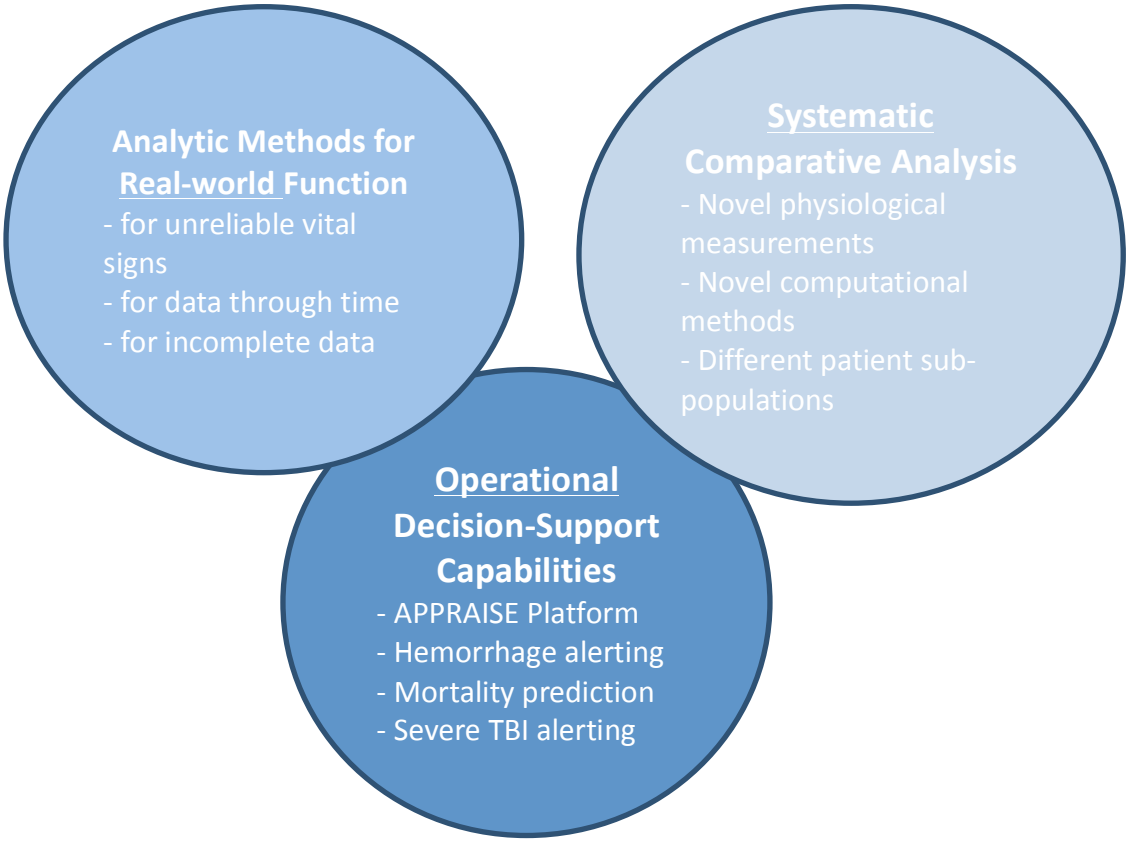
- Many of the measures are time sensitive. Yet, delaying initiation of the substantial bleeding protocol until after evaluation by a high-level specialist may result in preventable delays. For example, awaiting the evaluation of a trauma surgeon at the receiving hospital is at odds with the finding that the earlier plasma and platelets are received in the setting of substantial bleeding, the better the outcomes. Consider that the Stanford Medical Center [3] showed significant mortality benefit in a protocol that successfully reduced average time-to-first fresh frozen plasma (FFP) from 254 to 169 min. It seems entirely possible that FFP could be administered even earlier with potential to further benefit the patient.

- Activations of the protocols after arrival at the receiving facility forestall pre-hospital interventions specific to the substantially bleeding patient (i.e., pre-hospital practices that should only be applied to substantially bleeding patients but not to every trauma patient, either because the practices are too resource intensive or have an unfavorable risk-benefit profile in the non-bleeding patient).

1.3. Is it possible to use an automated pre-hospital alerting system for detecting patients at high risk of substantial bleeding?

Over the past decade, in close collaborator with the MRMC BHSAI, we have established that routine pre-hospital vital signs indicate trauma patients with substantial bleeding. This statement was based on a retrospective analysis of pre-hospital vital signs suggested that there were actionable patterns of hemorrhage common to trauma patients. We developed analytic algorithms that were able to automatically identify those patterns.

The current project is comprised of a prospective trial to validate whether, using automated decision-support algorithms, it is possible to identify trauma patients with substantial blood loss in real-time. Second, this project will deliver clinical validation for a suite of advanced physiologic sensors (being developed by Dr. Convertino's group, ISR), for purposes of transitioning the technology into actual prehospital operations.



BODY

In close collaborator with the MRMC BHSAI, we are working toward four sets of deliverables.

First, we are developing analytic methodologies that are effective during real-time performance. In the recent past, we have developed techniques for unreliable vital sign identification [8-10], decision-making of serial data through time [10,12-14], and incomplete data [11]. These capabilities are being validated through two investigational foci: prehospital [13] and within the MGH ED. As well, we are collaborating with the BHSAI to examine how these aforementioned techniques need to be customized to different environments (i.e., prehospital versus ED). We have completed our analysis of the prehospital dataset, and a report has been published [17]. In addition, we have collected a dataset with over 2000 ED trauma patients, and we have identified opportunities to make the analytic methodology even more clinically relevant. Specifically, we are modifying the APPRAISE hemorrhage identification algorithm. The original algorithm yielded a binary output (indicating whether or not the patient is likely bleeding). The modified algorithm yields the probability that the patient is bleeding, and the probability that any given life-saving intervention will be necessary for that patient.

Second, we have completed a set of comparative analyses. Collaborating with the BHSAI, we investigated whether heart rate variability enhanced routine vital signs [18], and whether the CareGuide muscle oxygenation sensor enhances routine vital signs [26]. We also examined different analytic techniques for detecting abnormalities in time-series data (such as the cumulative-sum versus sequential probability ratio test [12,16]). Overall, here were the major findings of the analysis:

- Almost all patients with major hemorrhage had patently abnormal vital signs *within 60 min* of monitoring (i.e., high sensitivity & high specificity using basic vital signs)
- Within the first hour, differentiation of patients with and without hemorrhage on the basis of routine vital signs was improved with the application of statistical algorithms
- Within the first hour, differentiation of patients with and without hemorrhage was also improved by tissue oximetery
- There was no *additional* diagnostic value in heart rate variability; SpO2 waveform analysis; vital sign trend analysis

Third, we are validating the overall clinical decision-making capabilities of these techniques. As noted, our prehospital real-time use results have been described in a manuscript [17]. We continue discussions with vendors about expanding the APPRAISE platform to prehospital monitors. Since the start of this project, we were awarded two US patents for this technology US 8,977,349 and 8,694,085. We have implemented a graphical user interface (GUI) for the system, which displays decision-support messages for supporting clinicians during the care of actual trauma patients. We have developed a methodology for validating the system, which involves both objective performance metrics as well as subjective case reviews by clinicians to identify whether there are any episodes whereby clinicians judge the system to be confusing or misleading. To this end, we have initiated the implementation of a database that will support multiple key needs: offline simulation testing of the new APPRAISE operational system; clinical validation (for regulatory approval) of the APPRAISE system; and a clinical trial studying the benefit of the system on the performance of the trauma team.

Finally, we are providing support for the FDA pre-submission application being prepared by the BHSAI. This support includes providing documentation, technical details, and technical review of the algorithm methodology, the validation methodology, potential regulatory claims, and the risk assessment.

KEY RESEARCH ACCOMPLISHMENTS

1. We have completed data analysis of our prehospital trial, and a manuscript that reports these findings has been accepted for publication in the journal SHOCK [17]. Briefly, we found that the hemorrhage identification algorithm performed as well in prospective real-time use on-board prehospital helicopters as it did in its earlier development phase. This supports the value of the technology for Combat Casualty Care.

2. In close collaboration with our TATRC/BHSAI colleagues, we published an analysis of the value of heart rate variability metrics for the identification of major hemorrhage in prehospital settings [18,19].

3. With our collaborators at TATRC/BHSAI, we reported a new analytic technique that uses routine vital signs to identify prehospital trauma patients with the highest risk of fatal traumatic brain injury [20]. This could be used for adjusting prehospital care protocols based on TBI risk, and could be used for mobilizing neurosurgical resources at the receiving facilities.

4. With our collaborators at TATRC/BHSAI, we have received two US patents for our computing platform, the APPRAISE system, "Collection and analysis of vital signs" (US Patent #8,694,085 and #8,977,349)

5. With our collaborators at TATRC/BHSAI, we have made a series of conference presentations about technical aspects of our work [21-26].

6. We have prepared an enhanced database of > 2,000 trauma patient physiological data, and associated clinical details and outcomes data, for algorithm assessment, which can be used for offline assessment of any investigational algorithm, e.g., heart rate variability, CRI, etc.

7. We completed Emergency Dept data collection for testing an investigational configuration of the advanced sensor suite (specifically, standard vitals signs plus muscle O2 saturation). We have reported the value of the CareGuide tissue sensor in trauma patients for early identification of life-threatening hemorrhage [27]. This manuscript was selected as key article for practicing clinicians in the prestigious New England Journal "Journal Watch" review.

8. We have designed and implemented an operational pilot graphical interface for the APPRAISE system. We have developed a testing protocol that has been approved by the local IRB, and passed the safety requirements of the hospital's biomedical engineering department. We have started analysis of this system's regulatory requirements for live-testing (i.e., with the display visible to the clinicians during care of trauma patients) with a focus on the US Food and Drug Administration which regulates medical devices.

9. We have completed our review of hemodymanic patterns in our database of > 2,000 trauma patient. We identified that there are no significant temporal trends in heart rate in trauma patients with life-threatening hemorrhage; that tachycardia is a weak but significant indicator of hemorrhagic injury; and that the vast majority of patients with life-threatening hemorrhage develop hypotension within 30 min from the onset of monitoring. This was published in the journal Injury [28].

10. We implemented and documented a database that will support multiple key needs: offline simulation testing of the new APPRAISE operational system; clinical validation (for regulatory approval) of the APPRAISE system; and a clinical trial studying the benefit of the system on the performance of the trauma team.

11. We supported the preparation of an FDA pre-submission application being prepared by the BHSAI. This support includes providing documentation, technical details, and technical review of the algorithm methodology, the validation methodology, potential regulatory claims, and the risk assessment.

REPORTABLE OUTCOMES

Below we report progress towards key outcomes.

Quarter 1:	In this quarter, we **added new pre-hospital patients transported to the BIDMC**; initiated our ED clinical study; and made progress on algorithm development (specifically for TBI).
Quarter 2:	In this quarter, we nearly completing chart review for the new pre-hospital patients transported to the BIDMC; screened our 98th subject for the Emergency Dept study; successfully worked with the vendor to enhance the investigational sensor, and prepared a report about our algorithm for TBI diagnosis using standard vital signs.
Quarter 3:	In this quarter, we focused on retrospective data analysis (i.e., analysis of vital sign patterns for TBI patients); ongoing clinical studies (i.e., data collection for Boston Medflight patients and data collection of MGH ED patients using the investigational muscle O2 sensor), and development of new technology (i.e., real-time vital sign analysis in the MGH ED).
Quarter 4	As of this quarter, prehospital data collection was **completed** and we undertook analysis (in collaboration with TATRC/BHSAI); analysis should be complete by next quarter and a manuscript submitted by the quarter thereafter; ED data collection continues successfully; our advancement plan suggests we will have a productive subsequent 12 months.
Quarter 5 (Year 2, Q1)	Prehospital data analysis is now largely complete and we are preparing reports and presentations of the findings which demonstrate that multivariate analysis of prehospital vital signs can identify patients with substantial bleeding long before arrival at the receiving facility; ED data collection continues to proceed as planned; in collaboration with BHSAI/TATRC, we have **successfully deployed** our real-time analysis system within the hospital Emergency Dept.
Quarter 6 (Year 2, Q2)	Prehospital data **analysis is complete** and a manuscript has been prepared for imminent submission. ED data collection proceeds and we have received approval for increasing the number of total subjects to ensure enough of the subjects have substantial bleeding. Preparation of reports has been a high-priority, spanning: *1*) diagnostic and prognostic value of the Glasgow Coma Scale for casualties with life-threatening traumatic brain injury (in submission);*2*) techniques for identifying abnormal patterns in time-series data (in preparation); *3*) comparative analysis of heart rate variability measures versus routine vital signs for the early identification of substantial bleeding (in preparation); and *4*) development and validation of the system for real-time analysis in the MGH ED (in preparation).
Quarter 7 (Year 2, Q3)	Prehospital data analysis is complete and a manuscript has been submitted. A second manuscript, about how a mathematical model can be used to assess for high-mortality traumatic brain injury on the basis of routine vital signs, **has been accepted to the Journal of Neurotrauma**. ED data collection proceeds and we expect to close enrollment in approximately 2 additional quarters. Preparation of reports has been a high-priority, spanning: *1*) techniques for identifying abnormal patterns in time-series data (in

	preparation); *2*) comparative analysis of heart rate variability measures versus routine vital signs for the early identification of substantial bleeding (in preparation); and *3*) development and validation of the system for real-time analysis in the MGH ED (in preparation); we anticipate these will be submitted in the upcoming quarter.
Quarter 8 (Year 2, Q4)	In terms of prehospital functionality, we have begun planning for a potential prospective, outcomes trial. For this, we have examined the data to better understand the APPRAISE system's functionality for patients who receive CPR (during a real-time trial, it will be important that the algorithm recognize when a patient is ineligible for automated hemorrhage identification, i.e., CPR) and we have held conversations with a potential industry partner, Zoll. **We received a US patent for our prehospital system US 8,694,085.** We have submitted three new papers (related to real-time analysis in the hospital; a comparison of different techniques for assessing continuous vital sign data to account for temporal variability that is unrelated to blood loss; and an examination of when, in trauma patients, the oscillation in sinus heart rate is coupled to respiration and when it is not.
Quarter 9 (Year 3, Q1)	This quarter, we have submitted a new paper (related to heart rate variability in identification of bleeding patients). Our prehospital report (about real-time vital signs automated analysis) is undergoing major revision at the behest of the journal editor. We have a total of 5 conference papers accepted this quarter: 3 papers accepted by the IEEE EMBC and 2 presentations accepted by MHSRS. We have collected CareGuide data in over 600 trauma patients and expect to complete subject enrollment in Sept 2014 (Quarter 10). We are engaged in discussions with MRMCs technology transfer office and Zoll medical about next steps for our hemorrhage detection algorithms.
Quarter 10 (Year 3, Q2)	This quarter, we have revised the two journal reports described in the prior quarter, and we await the decision of the journal reviewers and editors. We presented the 5 conference papers described in the prior quarter. We completed data enrollment for the CareGuide SmO2 sensor and we are undertaking analysis of the final results. We have commenced data collection for another 710 trauma subjects, archiving routine vital sign data for these patients, which will allow for testing of any algorithm that uses routine vital signs and/or pulse oximetry waveform analysis and/or heart rate variability analysis. We have proceeded to contract negotiations with Zoll medical for technology licensing and a cooperative research agreement.
Quarter 11 (Year 3, Q3)	This quarter, **the two journal reports described in the prior quarter were accepted for publication**. We have conducted data analysis on the CareGuide SmO2 sensor project described in the prior quarter, with plans to complete a manuscript in the next quarter. We have also worked with the vendor of CareGuide, RMI, to re-analyze our dataset using their reportedly improved SmO2 algorithm (for estimating SmO2 based on our pre-existing, archive of spectroscopy data from the CareGuide sensor in trauma patients).
Quarter 12 (Year 3, Q4)	This quarter, we prepared a manuscript about the CareGuide SmO2 sensor. As well, **we had two related conference presentations submitted and accepted**: to the annual Society of Academic Emergency Medicine (SAEM) meeting and the regional New England Research Directors' annual conference for SAEM. **We had a second patent awarded (Collection and analysis of vital signs US 8,977,349).** We have initiated data collection on physiological data

	for an additional 700 trauma patients within the Emergency Dept.
Quarter 13 (Year 4, Q1)	**The abstracts from Q12 were presented in this quarter**. The associated full journal manuscript was prepared and submitted, describing our experience evaluating the CareGuide tissue sensor in trauma patients. We initiated an enhanced, exhaustive investigation of automated statistical analysis for early detection and decision-support of trauma patients, seeking to validate the method throughout our complete archive of > 1,500 trauma patients.
Quarter 14 (Year 4, Q2)	**The manuscript (based on the abstracts presented in Q13) was accepted for publication in the peer-reviewed journal Academic Emergency Medicine.** We continue our enhanced investigation of automated statistical analysis of vital signs using our largest dataset; this will establish the version of the algorithm to be deployed in our outcomes trial. We have initiated development of the GUI, starting with defining the specifications, in close collaboration with BHSAI. We developed a prospective testing plan, in close collaboration with BHSAI.
Quarter 15 (Year 4, Q3)	Enhanced investigation of automated statistical analysis of vital signs has revealed two issues that need to be addressed prior to clinical deployment of the system. First, the SPRT results in a "persistence artifact" whereby low-level hemodynamic abnormalities will (given enough time) be determined to be hemorrhagic, even if the abnormality is mild and unchanging. Second, SPRT also causes latency that is an issue in the hospital, whereby hemorrhagic patients are frequently moved in-and-out of the resuscitation bay quickly, therefore its properties that were valuable during prehospital transport are potentially disadvantageous in the hospital. Based on the evaluation of this algorithm in > 1500 trauma patients, we have designed a modification to the algorithm which will give rise to the version 2.0. As well, we have recruited the software engineer and initiated design of the APPRAISE system for real-world clinical deployment.
Quarter 16 (Year 4, Q4)	We have developed a modified methodology for automated statistical analysis of vital signs. Preliminary testing (through simulation of real-time use, inputting archived trauma patient data from our curated dataset of > 1500 trauma patients) suggests that this methodology will enhance performance. We plan to finalize this analysis and document it in a peer-reviewed manuscript within the next quarter. In addition, we have made progress in the design and implementation of the APPRAISE system that is being built for true interaction with clinicians, i.e., clinicians will view the decision-support in real time and can use the information to potentially enhance patient care. Specifically, we have developed an implementation plan and initiated software coding, in consultation with our collaborators at the BHSAI.
Quarter 17 (Year 5, Q1)	This quarter has focused on preparations for deploying the real-time APPRAISE system with a goal for completing a functional system that is ready for deployment within Quarter 19 (noting that there are regulatory hurdles in terms of the hospital dept. of Biomed engineering and possibly IRB issues that may also affect the deployment date). The architecture of this system was finalized and implementation is underway, as is the v.0 version of the so-called message library of possible messages provided to caregivers. In parallel, we have examined the function of the new hemorrhage detection algorithm ("2.0") to examine, case-by-case in our dataset of >1800 trauma patients, what types of messages should be crafted. This will culminate in a manuscript ready for submission in Quarter 18.
Quarter 18 (Year 5, Q2)	Work continues as per Quarter 17. An initial version of the real-time system intended for testing has now been implemented and is undergoing reliability testing. The message library is being implemented into the real-time system. A clinical advisory group of physicians and nurses has been convened for ratifying the message library. A web-developer has been brought in to the program to improve the graphical user interface such that it is suitable for real-time clinical use. In parallel, the operation of the new hemorrhage detection algorithm ("2.0") has yielded a set of new results and authoring of a new report has been initiated.

Quarter 19 (Year 5, Q3)	The "alpha" version of the real-time APPRAISE system complete with GUI has been completed, including the graphical enhancements of the professional graphic designer. A protocol for testing this version (with clinicians blinded to the output) has been submitted to the IRB. The new hemorrhage detection algorithm has been further improved ("2.1") now including a new approach named the "time-adjusted binormal distribution" method and final validation is being completed of this algorithm, which is expected to lead to a journal report and possibly a patent application. **Another report, examining hemodynamic patterns during trauma patient deterioration, has been submitted for publication.**
Quarter 20 (Year 5, Q4)	The "alpha" version of the real-time APPRAISE system complete with GUI has been subjected to off-line non-clinical user acceptance reviews (a panel of clinicians including emergency medicine and trauma surgery, and including nurses and doctors-in-training), with important evolution of the system's specifications. Enhancements of the labeling and messages have been undertaken. As well, new enhancements, related to the necessity for clinicians to input information that is perceived as important by the panel, are being implemented. A revised algorithm optimized for real-time use is being implemented, in coordination with the MRMC BHSAI. The APPRAISE system was evaluated by the MGH Biomedical Engineering Dept. leading to safety requirements for both "blind" clinical testing (no display to clinicians) as well as future live clinical testing were developed. We are currently adapting the system to meet all safety requirements (related to issues such as network security, patient privacy, and electrical safety). We have also initiated planning for future necessary regulatory approvals, with a focus on the US FDA. The research report submitted last quarter, examining hemodynamic patterns during trauma patient deterioration, has been revised for publication.
Quarter 21 (Year 6, Q1)	The implementation of the revised algorithm (for detecting hemorrhage risk) has been completed and we are now initiating extensive validation of that new algorithm. As well, we have initiated redesign of the graphical user interface so that it is optimized for the characteristics of the new algorithm (which is based on risk strata, rather than a continuous output). We have initiated planning meetings to develop a regulatory clearance strategy, working closely with the USAMRMC BHSAI. We have initiated the implementation of a database that will support multiple key needs: offline simulation testing of the new APPRAISE operational system; clinical validation (for regulatory approval) of the APPRAISE system; and a clinical trial studying the benefit of the system on the performance of the trauma team. The research report being revised last quarter, examining hemodynamic patterns during trauma patient deterioration, has been completed and submitted for publication.
Quarter 22 (Year 6, Q2)	After revising the algorithm (now based on risk strata), we have started documenting its implementation and performance in a manner that is compliant with FDA regulations and software development standards. In parallel, we have invested significant effort to identify the optimal regulatory strategy. It should be understood that this level of specification and documentation of our system and preparation of the supporting clinical data is highly resource intensive. Specifically, we have begun exploring the potential claims for our software; how to validate those claims in an FDA-compliant manner (in terms of clinical investigation), how to scope the software (in terms of what functionality versus the trade-off of additional need for documentation/testing); and overall the documentation needed for our regulatory strategy. This has involved working with an FDA consultant. In parallel, we continue to work on the database started in the preceding quarter and the offline simulation started in the preceding quarter, and are on-track to complete these tasks in the first-half of the upcoming quarter.
Quarter 23 (Year 6, Q3)	A pilot system has been fully implemented including a revised graphical user display, a revised message engine/library of guidance messages, and a revised version of the hemorrhage-risk algorithm. This quarter was focused on revising the database of > 2000 trauma patients that is

	maintained in collaboration with the BHSAI, so that different parameters (from the individual datasets that make up the master database) are represented in consistent format, so that parameter values are verified, and so that parameter availability is documented and, if feasible, optimized by de novo chart review. The value of this new revised database is to enable a final phase of offline system software testing and validation, and user acceptance testing, which involves showing a panel of clinicians the various clinical situations and the output of the system through time, to ensure that the decision-support is always suitable for optimal patient care. We intend to conduct this final phase of testing (as well as associated software fixes and other optimizations) in the remainder of the funded time.
Quarter 24 (Year 6, Q4)	We completed reorganization and documentation of the previously collected datasets of vital signs and other clinical and outcome data from over 1500 trauma patients has been reorganized with improved annotation to allow improved simulation analysis of the APPRAISE system; specifically, studying minute-to-minute functionality and the clinical conditions and interventions associated with any unexpected system behavior. We started work to merge the software functionality that has been previously developed for bedside use and the hemorrhage risk assessment algorithm developed in the MATLAB environment. This has involved a new generation of "quality assurance" measures that are intended to suffice from a regulatory standpoint, for investigational human use and also obtaining 510(K) clearance for the software. This new functionality is generally more conservative, i.e., the algorithm is designed to become inoperable except when suitable data are available.

CONCLUSIONS

This technology development project is nearly complete, yielding a functional, well-validated system suitable for pilot testing during clinical care. Prehospital validation of the hemorrhage identification algorithm was a success, operating as specified. Two US patents have been awarded for the prehospital analysis system. A method for prehospital TBI assessment has been reported in the J Neurotrauma. A report about the validation of our prehospital system, APPRAISE, for detecting life-threatening hemorrhage was published. Our investigations have also shown that during the initial evaluation of actual trauma patients, a novel sensor, the CareGuide tissue oximeter, added significant diagnostic power beyond routine vital signs for identifying patients with life-threatening hemorrhage. We have now accumulated an archive of over 2000 trauma patients' electronic data, which is being used to enhance our decision-support algorithms. We studied patterns associated with hemorrhage, and have identified that almost all patients with life-threatening hemorrhage develop hypotension within 30 minutes of monitoring, whereas our technology can identify high-risk patients before the onset of hypotension. We have implemented a pilot GUI for the aforementioned APPRAISE system which can be used in a new series of clinical investigations whereby investigational decision-support is made visible to clinicians, to study whether this new generation of technology improves clinical management of trauma patients. We are on track for the USAMRMC BSHAI to have all the scientific and technical support necessary for their preparation and submission of a FDA pre-submission application by the end of this funded project.

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